

U.S. Patent Application No. 10/591,108  
Supplemental Preliminary Amendment

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**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) A compound of the formula (I)



or a pharmaceutically acceptable salt thereof, wherein

Z is selected from the group consisting of phenyl; naphthyl; indenyl; C<sub>3-7</sub> cycloalkyl; indanyl; tetralinyl; decalinyl; heterocycle; and heterobicycle, wherein Z is optionally substituted with one or more R<sup>8</sup>, wherein R<sup>8</sup> is independently selected from the group consisting of halogen; CN; OH; NH<sub>2</sub>; oxo (=O), where the ring is at least partially saturated; R<sup>9</sup>; and R<sup>10</sup>;

R<sup>9</sup> is selected from the group consisting of C<sub>1-6</sub> alkyl; O-C<sub>1-6</sub> alkyl; and S-C<sub>1-6</sub> alkyl, wherein R<sup>9</sup> is optionally interrupted by oxygen and wherein R<sup>9</sup> is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R<sup>10</sup> is selected from the group consisting of phenyl; heterocycle; and C<sub>3-7</sub> cycloalkyl, wherein R<sup>10</sup> is optionally substituted with one or more R<sup>11</sup>, wherein R<sup>11</sup> is independently selected from the group consisting of halogen; CN; OH; NH<sub>2</sub>; oxo (=O), where the ring is at least partially saturated; C<sub>1-6</sub> alkyl; O-C<sub>1-6</sub> alkyl; and S-C<sub>1-6</sub> alkyl;

R<sup>1</sup>, R<sup>4</sup> are independently selected from the group consisting of H; F; OH; and R<sup>4a</sup>;

R<sup>2</sup>, R<sup>5</sup> are independently selected from the group consisting of H; F; and R<sup>4b</sup>;

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$R^{4a}$  is independently selected from the group consisting of  $C_{1-6}$  alkyl; and  $O-C_{1-6}$  alkyl, wherein  $R^{4a}$  is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

$R^{4b}$  is  $C_{1-6}$  alkyl, wherein  $R^{4b}$  is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

$R^3$  is selected from the group consisting of H; and  $C_{1-6}$  alkyl;

Optionally one or more pairs of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$  independently selected from the group consisting of  $R^1/R^2$ ;  $R^2/R^3$ ;  $R^3/R^4$ ; and  $R^4/R^5$  form a  $C_{3-7}$  cycloalkyl ring, which is optionally substituted with one or more of  $R^{12}$ , wherein  $R^{12}$  is independently selected from the group consisting of F; Cl; and OH;

X is selected from the group consisting of  $S(O)$ ;  $S(O)_2$ ;  $C(O)$ ; and  $C(R^{13}R^{14})$ ;

$R^{13}$ ,  $R^{14}$  are independently selected from the group consisting of H; F;  $C_{1-6}$  alkyl;  $R^{15}$ ; and  $R^{16}$ ;

Optionally one or both pairs of  $R^5$ ,  $R^{13}$ ,  $R^{14}$  selected from the group consisting of  $R^5/R^{13}$ ; and  $R^{13}/R^{14}$  form a  $C_{3-7}$  cycloalkyl ring, which is optionally substituted with one or more  $R^{17}$ , wherein  $R^{17}$  is independently selected from the group consisting of F; Cl; and OH;

$R^{15}$  is selected from the group consisting of phenyl; naphthyl; and indenyl, wherein  $R^{15}$  is optionally substituted with one or more  $R^{18}$ , wherein  $R^{18}$  is independently selected from the group consisting of  $R^{19}$ ;  $R^{20}$ ; halogen; CN; COOH; OH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ;  $C_{1-6}$  alkyl;  $O-C_{1-6}$  alkyl;  $S-C_{1-6}$  alkyl;  $COO-C_{1-6}$  alkyl;  $OC(O)-C_{1-6}$  alkyl;  $C(O)N(R^{21})-C_{1-6}$  alkyl;  $S(O)_2N(R^{21})-C_{1-6}$  alkyl;  $S(O)N(R^{21})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{21})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{21})S(O)-C_{1-6}$  alkyl, wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

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$R^{16}$  is selected from the group consisting of heterocycle; heterobicycle;  $C_{3-7}$  cycloalkyl; indanyl; tertralinyl; and decaliny, wherein  $R^{16}$  is optionally substituted with one or more  $R^{22}$ , wherein  $R^{22}$  is independently selected from the group consisting of  $R^{18}$ ;  $R^{20}$ ; halogen; CN; OH; oxo (=O), where the ring is at least partially saturated;  $NH_2$ ; COOH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ;  $C_{1-6}$  alkyl; O- $C_{1-6}$  alkyl; S- $C_{1-6}$  alkyl;  $N(R^{23})-C_{1-6}$  alkyl; COO- $C_{1-6}$  alkyl; OC(O)- $C_{1-6}$  alkyl;  $C(O)N(R^{23})-C_{1-6}$  alkyl;  $N(R^{23})-C(O)-C_{1-6}$  alkyl;  $S(O)_2N(R^{23})-C_{1-6}$  alkyl;  $S(O)N(R^{23})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{23})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{23})S(O)-C_{1-6}$  alkyl, wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

$R^{19}$  is selected from the group consisting of phenyl; and naphthyl, wherein  $R^{19}$  is optionally substituted with one or more  $R^{24}$ , wherein  $R^{24}$  is independently selected from the group consisting of halogen; CN; COOH; OH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ;  $C_{1-6}$  alkyl; O- $C_{1-6}$  alkyl; S- $C_{1-6}$  alkyl; COO- $C_{1-6}$  alkyl; OC(O)- $C_{1-6}$  alkyl;  $C(O)N(R^{25})-C_{1-6}$  alkyl;  $S(O)_2N(R^{25})-C_{1-6}$  alkyl;  $S(O)N(R^{25})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{25})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{25})S(O)-C_{1-6}$  alkyl, wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

$R^{20}$  is selected from the group consisting of heterocycle; heterobicycle; and  $C_{3-7}$  cycloalkyl; wherein  $R^{20}$  is optionally substituted with one or more  $R^{26}$ , wherein  $R^{26}$  is independently selected from the group consisting of halogen; CN; OH; oxo (=O), where the ring is at least partially saturated;  $NH_2$ ; COOH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ;  $C_{1-6}$  alkyl; O- $C_{1-6}$  alkyl; S- $C_{1-6}$  alkyl;  $N(R^{27})-C_{1-6}$  alkyl; COO- $C_{1-6}$  alkyl; OC(O)- $C_{1-6}$  alkyl;  $C(O)N(R^{27})-C_{1-6}$  alkyl;  $N(R^{27})-C(O)-C_{1-6}$  alkyl;  $S(O)_2N(R^{27})-C_{1-6}$  alkyl;  $S(O)N(R^{27})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{27})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{27})S(O)-C_{1-6}$  alkyl wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

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$R^{21}$ ,  $R^{23}$ ,  $R^{25}$ ,  $R^{27}$  are independently selected from the group consisting of H; and  $C_{1-6}$ alkyl, which is optionally substituted with one or more of  $R^{28}$ , wherein  $R^{28}$  is independently selected from the group consisting of F; Cl and OH;

$R^6$ ,  $R^7$  are independently selected from the group consisting of H;  $(C(R^{29}R^{30}))_m-X^1-Z^1$ ;  $(C(R^{31}R^{32}))_n-X^2-X^3-Z^2$ ; and  $C_{1-4}$  alkyl, which is substituted with one or more  $R^{29a}$ , wherein  $R^{29a}$  is independently selected from the group consisting of  $R^{29b}$ ; and  $Z^1$ , provided that  $R^6$ ,  $R^7$  are selected so that not both of  $R^6$ ,  $R^7$  are independently selected from the group consisting of H;  $CH_3$ ;  $CH_2CH_3$ ;  $CH_2CH_2CH_3$ ; and  $CH(CH_3)_2$ ;

$R^{29}$ ,  $R^{29b}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$  are independently selected from the group consisting of H; halogen; CN; OH;  $NH_2$ ;  $COOH$ ;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ;  $C_{1-6}$  alkyl;  $O-C_{1-6}$  alkyl;  $N(R^{32a})-C_{1-6}$  alkyl;  $COO-C_{1-6}$  alkyl;  $OC(O)-C_{1-6}$  alkyl;  $C(O)N(R^{32a})-C_{1-6}$  alkyl;  $N(R^{32a})-C(O)-C_{1-6}$  alkyl;  $S(O)_2N(R^{32a})-C_{1-6}$  alkyl;  $S(O)N(R^{32a})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{32a})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{32a})S(O)-C_{1-6}$  alkyl wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

$R^{32a}$  is selected from the group consisting of H; and  $C_{1-6}$  alkyl, which is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

Optionally one or more pairs of  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$  independently selected from the group consisting of  $R^{29}/R^{30}$ ; and  $R^{31}/R^{32}$  form a  $C_{3-7}$  cycloalkyl ring, which is optionally substituted with one or more  $R^{32b}$ , wherein  $R^{32b}$  is independently selected from the group consisting of F; Cl; and OH;

m is 0, 1, 2, 3 or 4;

n is 2, 3 or 4;

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X<sup>1</sup> is independently selected from the group consisting of a covalent bond; -C<sub>1-6</sub> alkyl-; -C<sub>1-6</sub> alkyl-O-; -C<sub>1-6</sub> alkyl-N(R<sup>33</sup>)-; -C(O)-; -C(O)-C<sub>1-6</sub> alkyl-; -C(O)-C<sub>1-6</sub> alkyl-O-; -C(O)-C<sub>1-6</sub> alkyl-N(R<sup>33</sup>)-; -C(O)O-; -C(O)O-C<sub>1-6</sub> alkyl-; -C(O)O-C<sub>1-6</sub> alkyl-O-; -C(O)O-C<sub>1-6</sub> alkyl-N(R<sup>33</sup>)-; -C(O)N(R<sup>33</sup>)-; -C(O)N(R<sup>33</sup>)-C<sub>1-6</sub> alkyl-; -C(O)N(R<sup>33</sup>)-C<sub>1-6</sub> alkyl-O-; -C(O)N(R<sup>33</sup>)-C<sub>1-6</sub> alkyl-N(R<sup>34</sup>)-; -S(O)<sub>2</sub>-; -S(O)-; -S(O)<sub>2</sub>-C<sub>1-6</sub> alkyl-; -S(O)-C<sub>1-6</sub> alkyl-; -S(O)<sub>2</sub>-C<sub>1-6</sub> alkyl-O-; -S(O)-C<sub>1-6</sub> alkyl-O-; -S(O)<sub>2</sub>-C<sub>1-6</sub> alkyl-N(R<sup>33</sup>)-; and -S(O)-C<sub>1-6</sub> alkyl-N(R<sup>33</sup>)-; wherein each C<sub>1-6</sub> alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

X<sup>2</sup> is selected from the group consisting of -O-; -S-; -S(O)-; S(O)<sub>2</sub>-; and -N(R<sup>35</sup>)-;

X<sup>3</sup> is selected from the group consisting of a covalent bond; -C<sub>1-6</sub> alkyl-; -C<sub>1-6</sub> alkyl-O-; -C<sub>1-6</sub> alkyl-N(R<sup>36</sup>)-; -C(O)-; -C(O)-C<sub>1-6</sub> alkyl-; -C(O)-C<sub>1-6</sub> alkyl-O-; -C(O)-C<sub>1-6</sub> alkyl-N(R<sup>36</sup>)-; -C(O)O-; -C(O)O-C<sub>1-6</sub> alkyl-; -C(O)O-C<sub>1-6</sub> alkyl-O-; -C(O)O-C<sub>1-6</sub> alkyl-N(R<sup>36</sup>)-; -C(O)N(R<sup>36</sup>)-; -C(O)N(R<sup>36</sup>)-C<sub>1-6</sub> alkyl-; -C(O)N(R<sup>36</sup>)-C<sub>1-6</sub> alkyl-O-; and -C(O)N(R<sup>36</sup>)-C<sub>1-6</sub> alkyl-N(R<sup>37</sup>)-; wherein each C<sub>1-6</sub> alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

Optionally X<sup>2</sup>-X<sup>3</sup> are independently selected from the group consisting of -N(R<sup>35</sup>)-S(O)<sub>2</sub>-; -N(R<sup>35</sup>)-S(O)-; -N(R<sup>35</sup>)-S(O)<sub>2</sub>-C<sub>1-6</sub> alkyl-; -N(R<sup>35</sup>)-S(O)-C<sub>1-6</sub> alkyl-; -N(R<sup>35</sup>)-S(O)<sub>2</sub>-C<sub>1-6</sub> alkyl-O-; -N(R<sup>35</sup>)-S(O)-C<sub>1-6</sub> alkyl-O-; -N(R<sup>35</sup>)-S(O)<sub>2</sub>-C<sub>1-6</sub> alkyl-N(R<sup>36</sup>)-; and -N(R<sup>35</sup>)-S(O)-C<sub>1-6</sub> alkyl-N(R<sup>36</sup>)-; wherein each C<sub>1-6</sub> alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

R<sup>33</sup>, R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup> are independently selected from the group consisting of H; and C<sub>1-6</sub> alkyl, which is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

Z<sup>1</sup>, Z<sup>2</sup> are independently selected from the group consisting of Z<sup>3</sup>; and -C(R<sup>37a</sup>)Z<sup>3a</sup>Z<sup>3b</sup>;

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$R^{37a}$  is selected from the group consisting of H; and  $C_{1-6}$  alkyl, which is optionally substituted with one or more F;

$Z^3$ ,  $Z^{3a}$ ,  $Z^{3b}$  are independently selected from the group consisting of H;  $T^1$ ;  $T^2$ ;  $C_{1-6}$  alkyl;  $C_{1-6}$  alkyl- $T^1$ ; and  $C_{1-6}$  alkyl- $T^2$ ; wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more  $R^{37b}$ , wherein  $R^{37b}$  is independently selected from the group consisting of halogen; CN; OH;  $NH_2$ ; COOH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ;  $C_{1-6}$  alkyl; O- $C_{1-6}$  alkyl;  $N(R^{37c})-C_{1-6}$  alkyl; COO- $C_{1-6}$  alkyl; OC(O)- $C_{1-6}$  alkyl;  $C(O)N(R^{37c})-C_{1-6}$  alkyl;  $N(R^{37c})-C(O)-C_{1-6}$  alkyl;  $S(O)_2N(R^{37c})-C_{1-6}$  alkyl;  $S(O)N(R^{37c})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{37c})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{37c})S(O)-C_{1-6}$  alkyl; wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more halogen independently selected from the group consisting of F; and Cl;

$T^1$  is selected from the group consisting of phenyl; naphthyl; and indenyl; wherein  $T^1$  is optionally substituted with one or more  $R^{38}$ ; wherein  $R^{38}$  is independently selected from the group consisting of halogen; CN;  $R^{39}$ ; COOH; OH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ; COOT<sup>3</sup>; OT<sup>3</sup>; ST<sup>3</sup>;  $C(O)N(R^{40})T^3$ ;  $S(O)_2N(R^{40})T^3$ ;  $S(O)N(R^{40})T^3$  and T<sup>3</sup>;

$T^2$  is selected from the group consisting of  $C_{3-7}$  cycloalkyl; indanyl; tetralinyl; decalinyl; heterocycle; and heterobicycle; wherein  $T^2$  is optionally substituted with one or more  $R^{41}$ , wherein  $R^{41}$  is independently selected from the group consisting of halogen; CN;  $R^{42}$ ; OH; oxo (=O), where the ring is at least partially saturated;  $NH_2$ ; COOH;  $C(O)NH_2$ ;  $S(O)_2NH_2$ ;  $S(O)NH_2$ ; COOT<sup>3</sup>; OT<sup>3</sup>;  $C(O)N(R^{43})T^3$ ;  $S(O)_2N(R^{43})T^3$ ;  $S(O)N(R^{43})T^3$ ;  $N(R^{43})T^3$ ; and T<sup>3</sup>;

$R^{39}$  is selected from the group consisting of  $C_{1-6}$  alkyl; O- $C_{1-6}$  alkyl; S- $C_{1-6}$  alkyl; COO- $C_{1-6}$  alkyl; OC(O)- $C_{1-6}$  alkyl;  $C(O)N(R^{44})-C_{1-6}$  alkyl;  $S(O)_2N(R^{44})-C_{1-6}$  alkyl;  $S(O)N(R^{44})-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $N(R^{44})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{44})S(O)-C_{1-6}$  alkyl; wherein each  $C_{1-6}$  alkyl is optionally substituted with one more  $R^{45}$ , wherein  $R^{45}$  is independently selected from the group consisting of F; COOR<sup>46</sup>;  $C(O)N(R^{46}R^{47})$ ;  $S(O)_2N(R^{46}R^{47})$ ; OR<sup>46</sup>;  $N(R^{46}R^{47})$ ; T<sup>3</sup>; O-T<sup>3</sup>; and  $N(R^{46})-T^3$ ;

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$R^{42}$  is selected from the group consisting of  $C_{1-6}$  alkyl;  $O-C_{1-6}$  alkyl;  $S-C_{1-6}$  alkyl;  $N(R^{48})-C_{1-6}$  alkyl;  $COO-C_{1-6}$  alkyl;  $OC(O)-C_{1-6}$  alkyl;  $C(O)N(R^{48})-C_{1-6}$  alkyl;  $N(R^{48})-C(O)-C_{1-6}$  alkyl;  $S(O)_2N(R^{48})-C_{1-6}$  alkyl;  $S(O)N(R^{48})-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $-N(R^{48})S(O)_2-C_{1-6}$  alkyl; and  $-N(R^{48})S(O)-C_{1-6}$  alkyl; wherein each  $C_{1-6}$  alkyl is optionally substituted with one or more  $R^{45}$ , wherein  $R^{45}$  is independently selected from the group consisting of F;  $COOR^{49}$ ;  $C(O)N(R^{49}R^{50})$ ;  $S(O)_2N(R^{49}R^{50})$ ;  $S(O)N(R^{49}R^{50})$ ;  $OR^{49}$ ;  $N(R^{49}R^{50})$ ;  $T^3$ ;  $O-T^3$ ; and  $N(R^{49})-T^3$ ;

$R^{40}$ ,  $R^{43}$ ,  $R^{44}$ ,  $R^{46}$ ,  $R^{47}$ ,  $R^{48}$ ,  $R^{49}$ ,  $R^{50}$  are independently selected from the group consisting of H; and  $C_{1-6}$  alkyl;

$T^3$  is selected from the group consisting of  $T^4$ ; and  $T^5$ ;

$T^4$  is selected from the group consisting of phenyl; naphthyl; and indenyl; wherein  $T^4$  is optionally substituted with one or more  $R^{51}$ , wherein  $R^{51}$  is independently selected from the group consisting of halogen; CN;  $COOR^{52}$ ;  $OR^{52}$ ;  $C(O)N(R^{52}R^{53})$ ;  $S(O)_2N(R^{52}R^{53})$ ;  $C_{1-6}$  alkyl;  $O-C_{1-6}$  alkyl;  $S-C_{1-6}$  alkyl;  $COO-C_{1-6}$  alkyl;  $OC(O)-C_{1-6}$  alkyl;  $C(O)N(R^{52})-C_{1-6}$  alkyl;  $S(O)_2N(R^{52})-C_{1-6}$  alkyl;  $S(O)N(R^{52})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{52})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{52})S(O)-C_{1-6}$  alkyl; wherein each  $C_{1-6}$  alkyl is optionally substituted with one more halogen selected from the group consisting of F; and Cl;

$T^5$  is selected from the group consisting of heterocycle; heterobicycle;  $C_{3-7}$  cycloalkyl; indanyl; tetralinyl; and decalinyl; wherein  $T^5$  is optionally substituted with one or more  $R^{54}$ , wherein  $R^{54}$  is independently selected from the group consisting of halogen; CN;  $OR^{55}$ ; oxo (=O), where the ring is at least partially saturated;  $N(R^{55}R^{56})$ ;  $COOR^{55}$ ;  $C(O)N(R^{55}R^{56})$ ;  $S(O)_2N(R^{55}R^{56})$ ;  $S(O)N(R^{55}R^{56})$ ;  $C_{1-6}$  alkyl;  $O-C_{1-6}$  alkyl;  $S-C_{1-6}$  alkyl;  $N(R^{55})-C_{1-6}$  alkyl;  $COO-C_{1-6}$  alkyl;  $OC(O)-C_{1-6}$  alkyl;  $C(O)N(R^{55})-C_{1-6}$  alkyl;  $N(R^{55})-C(O)-C_{1-6}$  alkyl;  $S(O)_2N(R^{55})-C_{1-6}$  alkyl;  $S(O)N(R^{55})-C_{1-6}$  alkyl;  $S(O)_2-C_{1-6}$  alkyl;  $S(O)-C_{1-6}$  alkyl;  $N(R^{55})S(O)_2-C_{1-6}$  alkyl; and  $N(R^{55})S(O)-C_{1-6}$  alkyl; wherein each  $C_{1-6}$  alkyl is

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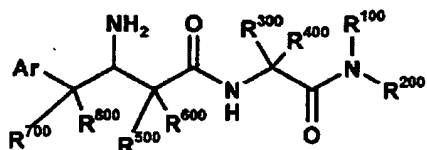
optionally substituted with one more halogen selected from the group consisting of F; and Cl;

$R^{52}$ ,  $R^{53}$ ,  $R^{55}$ ,  $R^{56}$ , are independently selected from the group consisting of H; and  $C_{1-6}$  alkyl;

with the proviso that the following compounds are excluded:

3-amino-N-cyclohexyl-4-phenyl-butyramide,  
(S)-3-amino-N-[5-(6-dimethylamino-purin-9-yl)-4-hydroxy-2-hydroxymethyl-tetrahydrofuran-3-yl]-4-p-tolyl-butyramide,  
(S)-2-((S)-2-amino-3-phenyl-propane-1-sulfonylamino)-3-phenyl-propionic acid,  
(S)-3-amino-4,N-diphenyl-butyramide;

and with the further proviso that compounds according to the following formula are excluded:



wherein

Ar is phenyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen;  $C_{1-6}$  alkyl optionally substituted with 1 to 5 halogens;  $O-C_{1-6}$  alkyl optionally substituted with 1 to 5 halogens; and cyano,

$R^{500}$ ,  $R^{600}$ ,  $R^{700}$ ,  $R^{800}$  are independently selected from H; and  $C_{1-6}$  alkyl, optionally substituted by 1 or 2 F,

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$R^{300}$  and  $R^{400}$  are independently selected from hydrogen;  $C_{1-6}$  alkyl, which is optionally substituted by 1 or 2 F; and  $C_{3-7}$  cycloalkyl, optionally substituted by 1, 2, 3, 4 or 5 substituents independently selected from halogen and hydroxy,

$R^{100}$  is selected from hydrogen; and  $C_{1-6}$  alkyl, optionally substituted by 1 or 2 F,

$R^{200}$  is selected from hydrogen;  $C_{1-6}$  alkyl;  $C_{3-7}$  cycloalkyl; phenyl; HET1;  $C_{1-6}$  alkylphenyl;  $-C_{1-6}$  alkylAR2;  $-C_{1-6}$  alkyl- $C_{3-7}$  cycloalkyl;  $-C_{1-6}$  alkyl-HET1;  $-C_{1-6}$  alkyl-HET2;  $-C_{1-6}$  alkyl- $CO_2C_{1-6}$  alkyl;  $-C_{1-6}$  alkylOCO- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylCO- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylNHCO- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylCONH-alkyl;  $-C_{1-6}$  alkylCON-di- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylNH- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylN-di- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylNHSO<sub>2</sub>- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylSO<sub>2</sub>NH- $C_{1-6}$  alkyl;  $-C_{1-6}$  alkylSO<sub>2</sub>- $C_{1-6}$  alkyl; and  $-C_{1-6}$  alkylSO<sub>2</sub>N-di( $C_{1-6}$ ) alkyl;

wherein each  $C_{1-6}$  alkyl is optionally substituted by 1 or 2 F; and

wherein phenyl, AR2, HET1, HET2 and  $C_{3-7}$  cycloalkyl are optionally substituted by 1, 2, 3, 4 or 5 substituents independently selected from phenyl (optionally substituted with halogen, trifluoromethyl,  $C_{1-4}$  alkyl or O- $C_{1-4}$  alkyl), halogen,  $C_{1-6}$  alkyl, halo $C_{1-6}$  alkyl, dihalo $C_{1-6}$  alkyl, trifluoromethyl, O- $C_{1-6}$  alkyl, carboxy- $C_{1-6}$  alkyl, carboxy- $C_{1-6}$  alkoxy, hydroxy, amino,  $C_{1-6}$  alkylamino, di $C_{1-6}$  alkylamino,  $-CONH_2$ ,  $-CONH-C_{1-6}$  alkyl,  $CON-di(C_{1-6})alkyl$ ,  $-NHCO-C_{1-6}$  alkyl,  $-SO_2-C_{1-6}$  alkyl,  $SO_2NH_2$ ,  $-SO_2NH-C_{1-6}$  alkyl,  $SO_2N-diC_{1-6}alkyl$  and  $-NHSO_2-C_{1-6}alkyl$ ,

further

$R^{100}$  and  $R^{200}$  may together with the nitrogen to which they are attached form a ring defined by HET1 or HET3,

wherein a ring comprising  $R^{100}$  and  $R^{200}$  is optionally substituted by 1 or 2 substituents independently selected from halogen,  $C_{1-6}$  alkyl, O- $C_{1-6}$  alkyl, cyano, carboxy, carboxy- $C_{1-6}$  alkyl,  $-CO_2-C_{1-6}$  alkyl,  $C_{1-6}$  alkylamino, di( $C_{1-6}$ ) alkylamino,  $-NHCO-C_{1-6}$  alkyl,  $-CONH-C_{1-6}$  alkyl,  $-CON-di-C_{1-6}$  alkyl and HET1, wherein each  $C_{1-6}$  alkyl group is optionally substituted by 1 or 2 substituents independently selected from hydroxy and fluoro;

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and

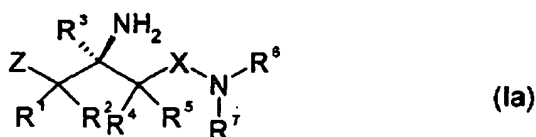
AR2 is a 8-, 9- or 10-membered unsaturated, partially or fully saturated bicyclic carbocyclic ring;

HET1 is a 3-, 4-, 5- or 6-membered, unsaturated, partially or fully saturated monocyclic heterocyclyl ring containing up to four heteroatoms independently selected from O, N, and S (but not containing any O-O, O-S or S-S bonds) linked via a ring carbon atom or a ring nitrogen atom if the ring is not thereby quaternised, and wherein an available carbon, sulfur or nitrogen atom may be oxidized;

HET2 is a 8-, 9- or 10-membered, unsaturated, partially or fully saturated bicyclic heterocyclyl ring containing up to four heteroatoms independently selected from O, N, and S (but not containing any O-O, O-S or S-S bonds) and linked via a ring carbon atom in either of the rings comprising the bicyclic system; and

HET3 is a N-linked saturated bicyclic ring system containing up to 12 ring atoms including the linking nitrogen atom.

2. (Original) A compound according to claim 1 of formula (Ia)



or a pharmaceutically acceptable salt thereof, wherein Z, R<sup>1</sup>-R<sup>7</sup> and X have the meaning as indicated in claim 1.

3. (Previously presented) A compound according to claim 1, wherein Z is phenyl or heterocycle.

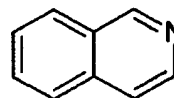
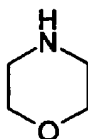
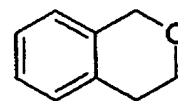
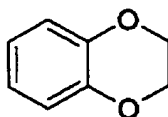
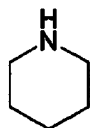
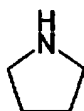
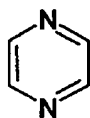
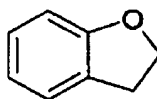
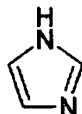
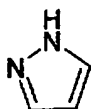
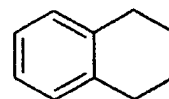
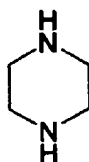
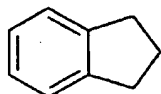
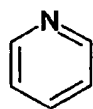
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4. (Previously presented) A compound according to claim 1, wherein Z is optionally substituted with 1 or 2 R<sup>8</sup>, which are the same or different.
5. (Previously presented) A compound according to claim 1, wherein R<sup>8</sup> is selected from the group consisting of Cl; F; CN; CH<sub>3</sub>; and OCH<sub>3</sub>.
6. (Previously presented) A compound according to claim 1, wherein Z is 2-Fluorophenyl.
7. (Previously presented) A compound according to claim 1, wherein R<sup>1</sup>, R<sup>4</sup> are independently selected from the group consisting of H; F; OH; CH<sub>3</sub>; and OCH<sub>3</sub>.
8. (Previously presented) A compound according to claim 1, wherein R<sup>2</sup>, R<sup>5</sup> are independently selected from the group consisting of H; F; and CH<sub>3</sub>.
9. (Previously presented) A compound according to claim 1, wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup> are H.
10. (Previously presented) A compound according to claim 1, wherein R<sup>3</sup> is H.
11. (Previously presented) A compound according to claim 1, wherein X is C(O) or S(O)<sub>2</sub>.
12. (Previously presented) A compound according to claim 1, wherein R<sup>6</sup> is selected from the group consisting of H; and CH<sub>3</sub>.
13. (Previously presented) A compound according to claim 1, wherein X<sup>1</sup> is a covalent bond.

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14. (Previously presented) A compound according to claim 1, wherein  $m$  is 0, 1, 2 or 3.
15. (Previously presented) A compound according to claim 1, wherein  $R^7$  is  $Z^1$ .
16. (Previously presented) A compound according to claim 1, wherein  $R^7$  is  $C_{1-4}$  alkyl, substituted with 1-4  $R^{28a}$ , which are the same or different.
17. (Original) A compound according to claim 16, wherein  $R^7$  is selected from the group consisting of  $CH(R^{29a})_2$ ;  $CHR^{28a}-CH_2R^{28a}$ ;  $CH_2-CH(R^{29a})_2$ ;  $CH_2-CHR^{29a}-CH_2R^{29a}$ ; and  $CH_2-CH_2-CH(R^{29a})_2$ .
18. (Previously presented) A compound according to claim 1, wherein  $R^{29a}$  is selected from the group consisting of  $R^{29b}$ ; and  $Z^1$ ; and wherein  $R^{29b}$  is selected from the group consisting of H; F; Cl;  $NH_2$ ;  $NHCH_3$ ;  $N(CH_3)_2$ ;  $CH_3$ ; and  $C_2H_5$ .
19. (Previously presented) A compound according to claim 1, wherein  $R^{29a}$  is selected from the group consisting of  $R^{29b}$ ; and  $Z^1$ ; and wherein  $Z^1$  is selected from the group consisting of  $T^1$ ; and  $T^2$ .
20. (Previously presented) A compound according to claim 1, wherein  $T^1$  is phenyl; and wherein  $T^1$  is optionally substituted with 1-3  $R^{38}$ , which are the same or different.
21. (Previously presented) A compound according to claim 1, wherein  $R^{38}$  is independently selected from the group consisting of F; Cl; CN;  $CH_3$ ;  $C_2H_5$ ;  $CH_2CH_2CH_3$ ;  $CH(CH_3)_2$ ;  $CF_3$ ;  $O-CH_3$ ;  $O-C_2H_5$ ;  $S-CH_3$ ;  $SO_2NH_2$ ;  $T^3$ ; and  $O-T^3$ .
22. (Previously presented) A compound according to claim 1, wherein  $T^2$  is selected from the group consisting of

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and wherein  $T^2$  is optionally substituted with 1-2  $R^{41}$ , which are the same or different.

23. (Previously presented) A compound according to claim 1, wherein  $R^{41}$  is selected from the group consisting of OH;  $CH_3$ ; and  $T^3$ ;

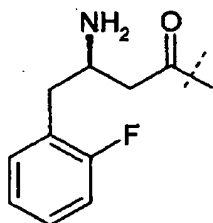
24. (Previously presented) A compound according to claim 1, wherein  $T^3$  is  $T^4$ .

25. (Previously presented) A compound according to claim 1, wherein  $T^4$  is phenyl, wherein  $T^4$  is optionally substituted with 1-3  $R^{51}$ , which are the same or different.

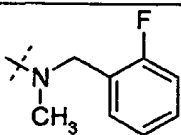
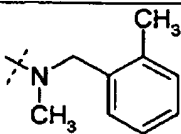
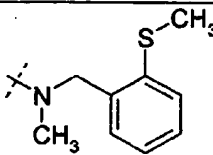
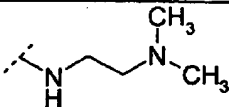
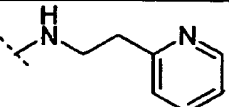
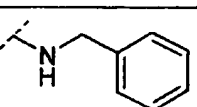
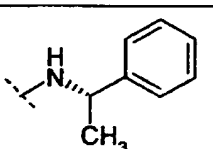
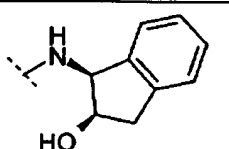
26. (Previously presented) A compound according to claim 1, wherein  $R^{51}$  is independently selected from the group consisting of F; Cl;  $CH_3$ ;  $C_2H_5$ ;  $CH_2CH_2CH_3$ ;  $CH(CH_3)_2$ ;  $CF_3$ ; O- $CH_3$ ; O- $C_2H_5$ ; S- $CH_3$ ; and  $SO_2NH_2$ .

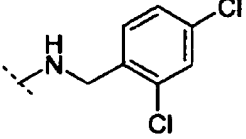
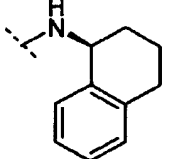
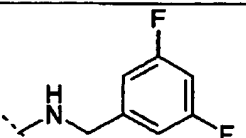
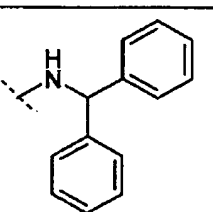
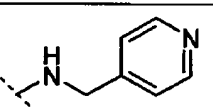
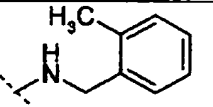
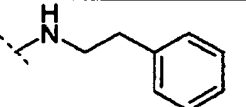
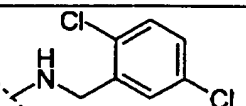
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27. (Previously presented) A compound according to claim 1, wherein  $T^3$  is  $T^5$ .
28. (Previously presented) A compound according to claim 1, wherein  $T^5$  is heterocycle, wherein  $T^5$  is optionally substituted with 1-2  $R^{54}$ , which are the same or different.
29. (Previously presented) A compound according to claim 1, wherein  $R^{54}$  is selected from the group consisting of OH; and  $CH_3$ .
30. (Original) A compound according to claim 1 selected from the group consisting of

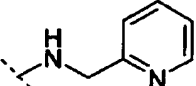
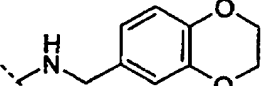
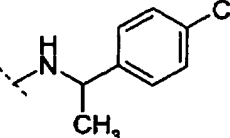
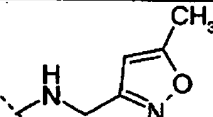
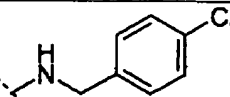
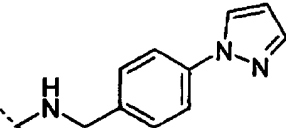
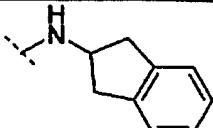
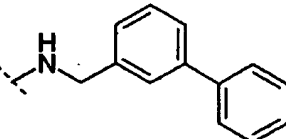
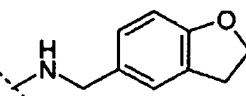
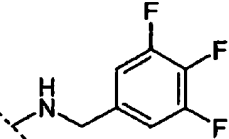
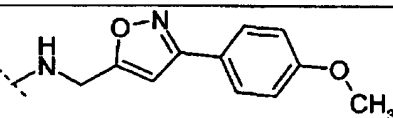
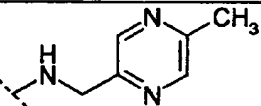
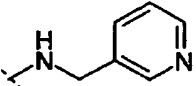
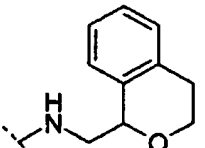
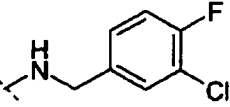
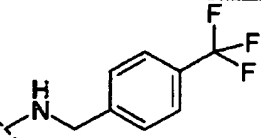
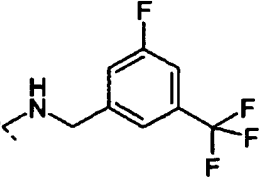


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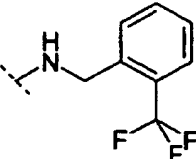
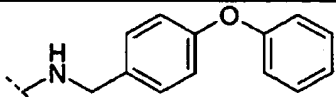
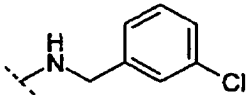
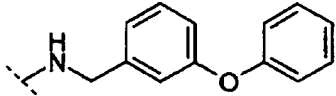
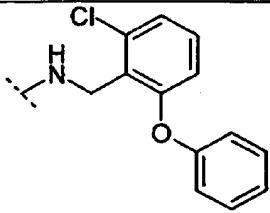
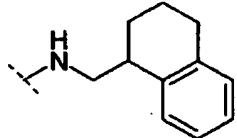
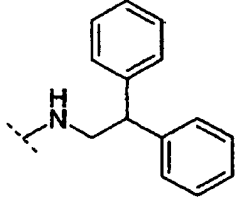
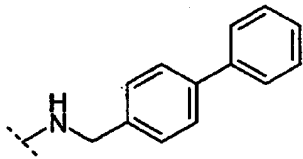
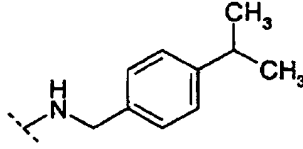
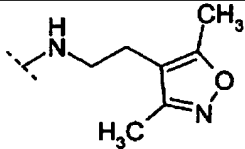
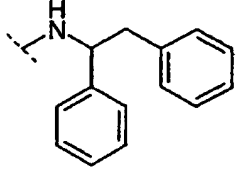
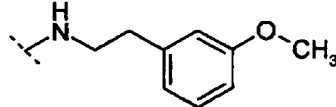
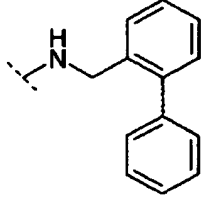
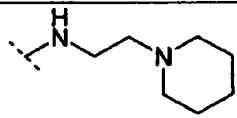
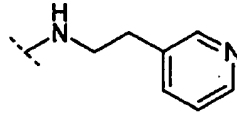
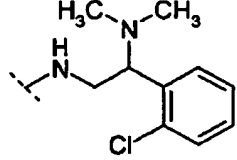
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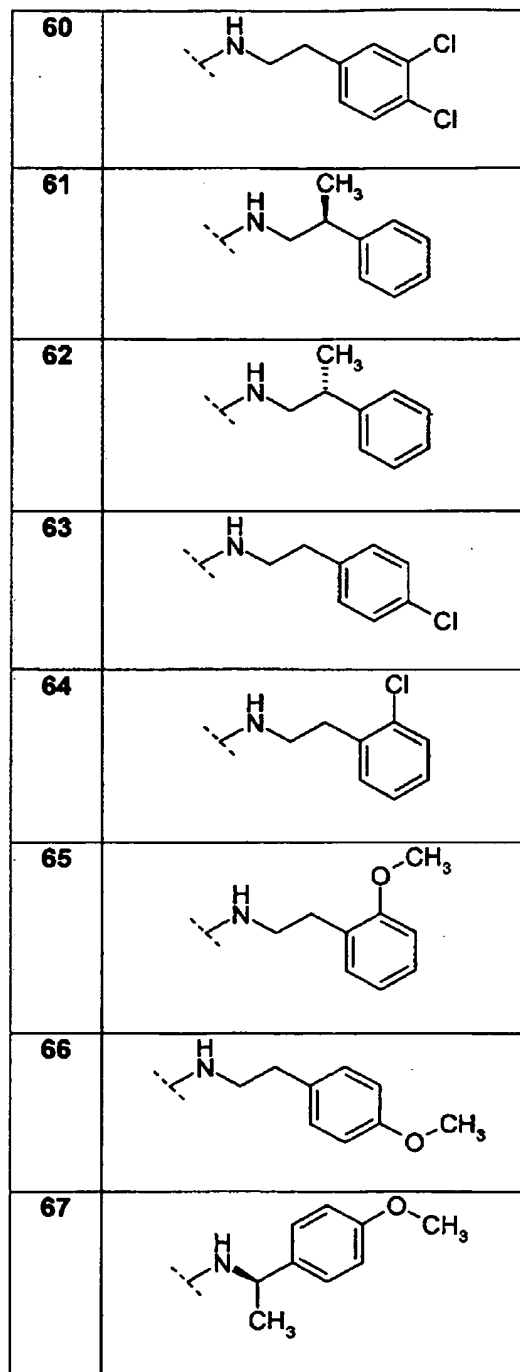
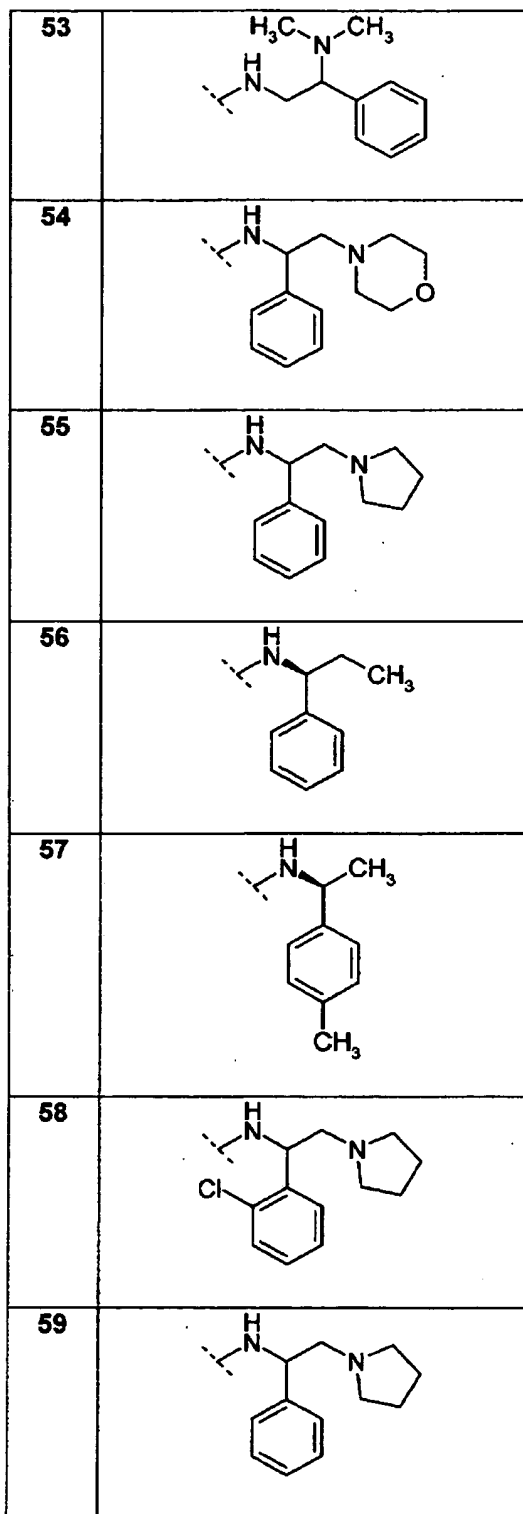
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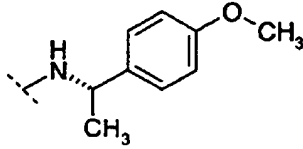
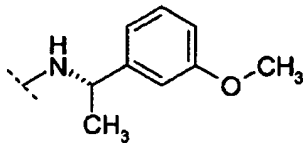
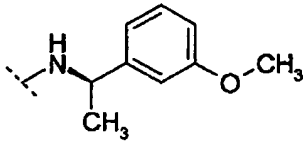
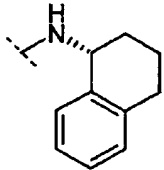
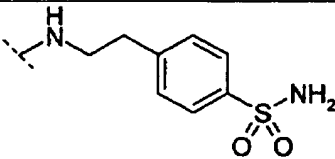
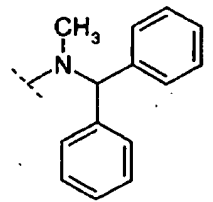
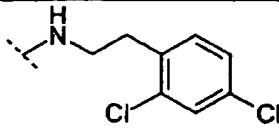
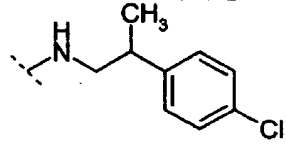
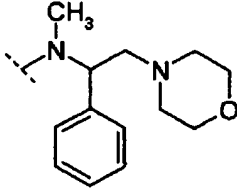
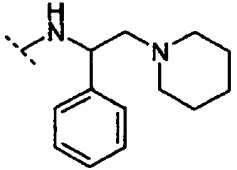
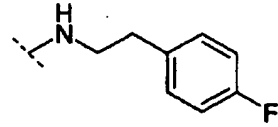
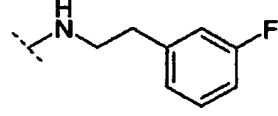
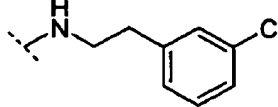
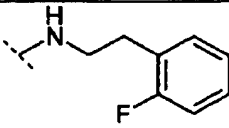
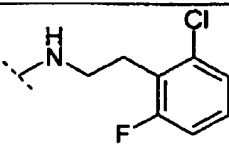
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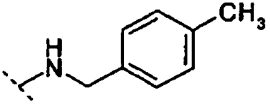
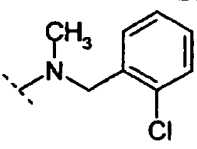
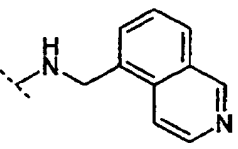
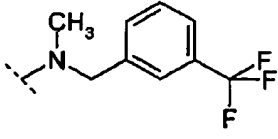
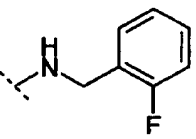
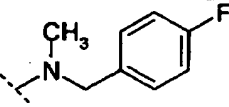
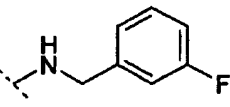
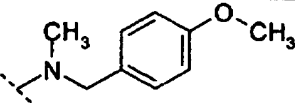
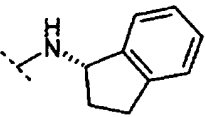
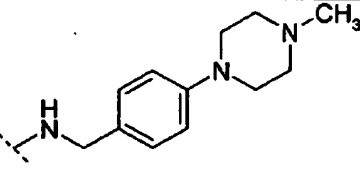
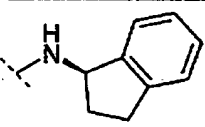
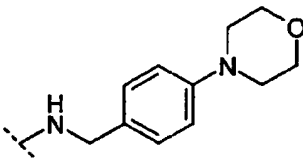
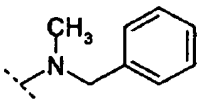
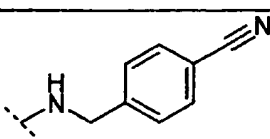
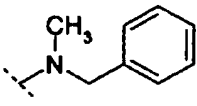
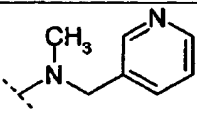
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31. (Previously presented) A prodrug compound of a compound according to claim 1.
32. (Currently amended) A pharmaceutical composition comprising said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof according to claim 1 together with a pharmaceutically acceptable carrier.
33. (Currently amended) A pharmaceutical composition according to claim 32, comprising one or more additional compounds or pharmaceutically acceptable salts thereof selected from the group consisting of another of said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof; another DPP-IV inhibitor; insulin sensitizers; PPAR agonists; biguanides; protein tyrosinephosphatase-1B (PTP-1B) inhibitors; insulin and insulin mimetics; sulfonylureas and other insulin secretagogues;  $\alpha$ -glucosidase inhibitors; glucagon receptor antagonists; GLP-1, GLP-1 mimetics, and GLP-1 receptor agonists; GIP, GIP mimetics, and GIP receptor agonists; PACAP, PACAP mimetics, and PACAP receptor 3 agonists; cholesterol lowering agents; HMG-CoA reductase inhibitors; sequestrants; nicotiny alcohol; nicotinic acid or a salt thereof; PPAR $\alpha$  agonists; PPAR $\alpha$ / $\gamma$  dual agonists; inhibitors of cholesterol absorption; acyl CoA : cholesterol acyltransferase inhibitors; anti-oxidants; PPAR $\alpha$  agonists; antiobesity compounds; an ileal bile acid transporter inhibitor; and anti-inflammatory agents.
34. (Currently amended) A compound or a pharmaceutically acceptable salt thereof or a prodrug thereof of claim 1 for use as a medicament.
35. (Currently amended) A method for the treatment or prophylaxis of non-insulin dependent (Type II) diabetes mellitus; hyperglycemia; obesity; insulin resistance; lipid disorders; dyslipidemia; hyperlipidemia; hypertriglyceridemia; hypercholesterolemia; low HDL; high LDL; atherosclerosis; growth hormone deficiency; diseases related to the immune response; HIV infection; neutropenia; neuronal disorders; tumor metastasis; benign

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prostatic hypertrophy; gingivitis; hypertension; osteoporosis; diseases related to sperm motility; low glucose tolerance; insulin resistance; its sequelae; vascular restenosis; irritable bowel syndrome; inflammatory bowel disease; including Crohn's disease and ulcerative colitis; other inflammatory conditions; pancreatitis; abdominal obesity; neurodegenerative disease; anxiety; depression; retinopathy; nephropathy; neuropathy; Syndrome X; ovarian hyperandrogenism (polycystic ovarian syndrome; Type II diabetes; or growth hormone deficiency, comprising administering to a subject in need of said treatment said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof of claim 1.

36. (Currently amended) A method to inhibit DPP-IV peptidase activity comprising administering said compound or said pharmaceutically acceptable salt thereof or a prodrug thereof of claim 1 to a subject in an amount sufficient to inhibit DPP-IV peptidase activity.